#18

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/868,987 | MURDIN ET AL. | |
| | Examiner | Art Unit | |
| | Padmavathi v Baskar | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-39,79 and 80* is/are pending in the application.

4a) Of the above claim(s) *20-24, 26-35, 36, 37, 38 (b), 38 (c) and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1- 19, 25, 36, 38 (a), 79 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-39,79 and 80* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## Response to Amendment

1. Applicant's amendment filed on 6/27/03 (paper # 14) is acknowledged. Claims 2, 8-14, 16, 18, 19 and 36 have been amended.

2. The numbering of claims is not accordance with 37 CFR 1.126, which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 40 and 41 have been renumbered as 79-80 respectively and are entered.

Claims 1-39, 79 and 80 are pending in the application.

3. The examiner acknowledges the various amendments made to the specification in response to the previous Office action.

4. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

## *Priority*

5. The examiner indicated in the previous Office action, (Paper # 12) that priority is being claimed to a large number of provisional applications,

(This application is a national stage entry of PCT/CA99/01230 12/23/1999

Which Claims Priority from Provisional Application 60113280

Which Claims Priority from Provisional Application 60113281

Which Claims Priority from Provisional Application 60113282

Which Claims Priority from Provisional Application 60113283

Which Claims Priority from Provisional Application 60113284

Which Claims Priority from Provisional Application 60113285

Which Claims Priority from Provisional Application 60114050

Which Claims Priority from Provisional Application 60114056

Which Claims Priority from Provisional Application 60114057

Which Claims Priority from Provisional Application 60114058

Which Claims Priority from Provisional Application 60114059

Which Claims Priority from Provisional Application 60114061)

and these applications appear to be drawn to unrelated subject matter and are either not available for consideration or for which consideration to determine support for the instantly claimed subject matter would require an undue burden. Therefore, the elected claims, drawn to SEQ ID NO: 1 have an effective filing date of 12/23/1999.

In response to that Office action, (Paper # 12), the applicant has now (amendment filed on 6/27/03 paper # 14) identified Provisional Application 60113281 (filed on 12/23/1998) as a priority document and showed support for the elected invention. Therefore, the priority is accorded as of the filing date of the provisional application, 12/23/1998.

6. In view of the petition decision, Claims 1- 19, 25, 36, 38 (a), 79 and 80, drawn to DNA are under prosecution with respect to DNA comprising SEQ.ID.NO: 1 and DNA encoding SEQ ID No 14.

7. Claims 20-24, 26-35, 36, 37, 38 (b), 38 (c) and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

**Rejections withdrawn.**

8. Since priority date is accorded as of 12/23/1998 in this office action, Kalman et al, (Accession No: AE001641'Nat. Genet. 1999, 21(4): 385-389) is no longer applicable as a prior art. Hence, the rejection under 35 U.S.C 102(b) is withdrawn.

9. In view of the amendments to the claims, the rejection under 35 U.S.C. 101 is withdrawn

10. In view of the abandonment of the pending application 09/886, 468, the rejection under the judicially created doctrine of obviousness-type double patenting is withdrawn. Applicant is advised to send a copy of the abandonment of application 09/886, 468 so that the record is complete.

11. In view of the amendments to the claims, the rejection under 35 U.S.C. 112, second paragraph is withdrawn.

***Claim Rejections - 35 USC § 112***

12. Claims 1-19, 36, 38(a), 79 and 80 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov) This is a written description rejection.

The specification only describes a polynucleotide sequence of SEQ ID NO: 1. The specification describes as part of the invention-isolated polynucleotide encoding the polypeptide of SEQ ID NO: 14 (CPN 100686 RY 54), which is a "putative 98kDouter membrane protein (see pages 8-10). However, broadly claimed nucleic acid sequence which encodes a polypeptide which is at least 75% identical to amino acid sequence to SEQ.ID.NO: 14, a nucleic acid comprising 38 consecutive nucleic acids, a nucleic acid sequence encoding an immunogenic fragments of 50 or 12 consecutive amino acids and a method of preventing infection using such nucleic acid is not set forth in this specification. Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides by use of language in which a specified percent of amino acids can be

changed. As depending from these are the vectors, host cells, vaccines, diagnostics and methods of producing the polypeptide. None of these sequences meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequence consisting of SEQ ID NO: 1 which corresponds to the polynucleic acid sequence encoding the Chlamydia pneumoniae protein which comprises SEQ ID N0: 14. Thus, an isolated polynucleotide sequence comprising of SEQ ID NO: 1 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The claimed properties of the putative 98 kD protein can only be determined empirically by actually making every nucleic acid that encodes the recited variability (i.e. the instant 75% identity) and testing each to determine whether it encodes a protein having the particularly disclosed properties of an 98kDprotein. As noted in the Guidelines at Section I.A (2). There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. There is no written description support for a method of preventing Chlamydial infection as claimed.

Applicants specification proposes the converse, yet still does not meet the requirements for an adequate written description of the claimed invention. Applicants propose that the skilled artisan is to modify a known nucleic acid sequence encoding a known protein sequence and that modification would still describe applicants invention as a 98kDprotein as disclosed. The 98kD outer membrane protein is uncharacterized by this specification and is not asserted to belong to any known family of proteins. The protein has specific biological properties dictated by the structure of the protein and the corresponding structure of the structural gene sequence which encodes it. There must be some nexus between the structure of a gene sequence and the structure of the protein encoded, and the function of that encoded protein. However, similar function cannot be predicted from the modification of the structure of the gene or in this case the gene encoding the protein. Applicants have not shown that, by modifying a reference sequence encoding a reference polypeptide as claimed, will automatically predict the production of a 98kDouter membrane protein as disclosed. While it is true that, due to the nature of codon degeneracy, applicant may take a reference sequence and modify that sequence to be a different nucleic acid sequence, yet still have that nucleic acid encode the same putative 98 kD protein. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of a representative number of polynucleotides encoding a representative number 98kDpolypeptides, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. With the exception of an isolated polynucleotide comprising SEQ ID NO: 1 and an isolated polynucleotide comprising of a nucleotide sequence encoding SEQ ID NO: 14, fragments thereof and associated, vectors, vaccines, fusions etc dependent thereon, the skilled artisan cannot envision the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless

of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Applicant's arguments filed on 6/27/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that the specification on pages 19 and 12 fully describe the claimed immunogenic fragments or a sequence, which encodes a 75% identical polypeptide. The examiner reviewed the cited pages and found no specific support for the claimed invention. Further applicant argues that the present invention is not related to Eli Lilly and Amgen and not claiming a chemical compound by name and hoped for function as in Eli Lilly, or a mere elucidation of a research plan to obtain a chemical compound described by name only as in Amgen. Applicant further states that the specification clearly describes the claimed fragments and variants.

The examiner disagrees with the applicant because applicant indeed is claiming a compound product such as immunogenic fragment comprising 12 amino acids or 50 amino acids or a peptide having 75% identity with SEQ.ID.NO: 1 by name/numbers without a function like Eli Lilly. Similarly, applicant is claiming a compound fragments like Amgen in describing general techniques in the art without a specific property.

13. Claims 1-19, 36, 38 (a), 79 and 80 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising SEQ ID NO: 1, DNA encoding SEQ.ID.NO: 14, vector comprising said nucleic acid, and host cell comprising said vector, the specification does not reasonably provide enablement for any nucleic acid encoding immunogenic fragments or pharmacological composition comprising said

fragments of SEQ.ID.NO: 1 or encoding fragments of SEQ.ID.NO: 14, immunogenic fragments comprising a nucleic acid encoding 12 or 50 amino acid and a sequence which encodes a 75% identical polypeptide variant thereof and a method of preventing Chlamydial infection using said fragment nucleic acids.

Applicant's arguments filed on 6/27/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that the specification is fully enabled for the claimed variants or fragments without undue experimentation one skilled in the art can make and use the claimed invention and gives the In re wands analysis. Applicant cites several general protocols obtained from Web sites and provides case laws to support the claimed fragments or variants are fully enabled and the examiner should withdrawn the scope of enablement rejection.

The examiner has reviewed the Web sites and also other available art regarding protein chemistry and disagrees with the applicant because

The state of the prior art indicates that protein chemistry is probably one of the most unpredictable areas of biotechnology and is highly complex. As taught by the prior art (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6), the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis. The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or

asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67) teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition.

***Claim Rejections - 35 USC 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an

international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 18-19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Boehringer Mannheim Biochemicals (1991 Catalog page 557), Stratagene (1991 Product Catalog, page 66), Gibco BRL (Catalogue & Reference Guide 1992, page 292), Promega (1993/1994 Catalog, pages 90-91) or New England BioLabs (Catalog 1986/1987, pages 60- -- 62).

Gibco BRL (Catalogue & Reference Guide 1992, page 292), Promega (1993/1994 Catalog, pages 90-91) or New England BioLabs (Catalog 1986/1987, pages 60-62) each disclose a wide variety of probes, primers of over 10 nucleotides in length. Thus the disclosed random primers, probes anticipated the instant claims. The primers have been applied as relevant to the restriction map provided for SEQ ID NO: 1.

Boehringer Mannheim Biochemicals (1991 Catalog page 557), Stratagene (1991 Product Catalog, page 66), disclose kits containing isolated packaged random 6-mer primers and random 9-mer primers. The random primer kits contain all possible 6 mer and 9 mer sequences for priming DNA sequences for labeling. The prior art anticipated the claimed invention.

Applicant states that none of the cited references disclose the elements of the claims because a purified probe or a primer have not explicitly disclose the sequences that can be compared with the sequences of claims 18 and 19. Applicant further states, Examiner might have rejected the claims based on inherency.

The examiner has not rejected claims based on inherency but clearly indicated that the random primer kits contain all possible 6 mer and 9 mer sequences for priming DNA sequences for labeling are widely available in the market. For example see Promega Catalogue discloses 8mer GGAATTCC that hybridizes with SEQ.ID.NO; 1 at position approximately between 880-900. Further these probes are isolated and labeled.

16. Claims 1, 2, 8, 16, 38 and 79-80 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Griffais U.S.Patent 6, 559, 294.

As the priority is accorded to this application as of the filing date of the provisional application, 12/23/1998, Griffais filed on 11/23/1998 is 102 (e) art. This reference should have been 102 (b) as this application gets foreign priority as of 11/21/1997. However, the examiner is unable to locate the application 09/198,452 (U.S.Patent 6, 559, 294). Therefore, the examiner is using the filing date of this application 11/23/1998 as 102 (e) date.

(The examiner is viewing the composition and kit claims as intended use of the claimed invention, isolated nucleic acid molecule)

Griffais U.S.Patent 6, 559, 294 discloses a nucleic acid sequence (SEQ.ID.NO: 1, see the sequence alignment) from C. pneumoniae which encodes a polypeptide SEQ.ID.NO: 14, immunogenic fragment comprising at least 50 consecutive amino acids, nucleic acid molecule comprising 38 consecutive nucleotides (see the sequence alignment) and is 98.3 % identical to SEQ ID NO: 14. Therefore, the prior art meets the limitations of claimed nucleic acid molecule. The prior art anticipated the claimed invention.

***Status of Claims***

17. No claims are allowed.

***Conclusion***

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

L. F. Smith

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